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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,303	11/21/2001	Paul A.E. Piunno	99-00	5364

23713 7590 02/19/2004

GREENLEE WINNER AND SULLIVAN P C
5370 MANHATTAN CIRCLE
SUITE 201
BOULDER, CO 80303

EXAMINER	
SAKELARIS, SALLY A	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 02/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,303	PIUNNO ET AL.	
	Examiner	Art Unit	
	Sally A Sakelaris	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-77* is/are pending in the application.

4a) Of the above claim(s) *25-71, and 75-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24 and 72-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/4/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-24 and 72-74 is acknowledged. Applicant's arguments filed 1/26/04 have been fully considered but they are not persuasive. The traversal is on the ground(s) that the office has mischaracterized the relationship between the inventions of Groups I-III. Applicant asserts that the method of making, and the method of using the product of group I are both linked to the product and should be considered as linking claims. However the examiner disagrees as each of these inventions are patentably distinct as previously shown in the restriction requirement sent 8/26/2003, and as such have been separated as prescribed in MPEP § 806.05(h) and under 35 U.S.C. § 121, as the presently written claims are not viewed as linking claims. Applicant is reminded that:

> The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.
>
> In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended

during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Furthermore, applicant traverses on the grounds that the groups of claims are related by the overlapping class and subclass groups into which the claims are classified. However, the search and examination of all possible groups would pose an enormous burden on the examiner and on the PTO search resources. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as demonstrated by their recognized divergent subject matter since all of the methods would require different searches that are not coextensive, examination of these claims would pose a serious burden on the examiner and therefore the restriction is deemed proper and is made final. The examiner maintains the restriction requirement made previously, as each group is correctly separated as unrelated or patentably distinct.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. The present application's claim to benefit of a U.S. provisional Application 60/252643 filed November 21, 2000, is granted.

Claims Interpretations

It should be noted that the terms, "fully-matched", "mismatched", "low immobilization density", "medium-high immobilization density", and "high immobilization density" are not defined to provide an actual structural requirement to the claims. As a result, little weight will be

given to these terms in the office's rejection of these claims with the prior art. Applicant should note that with respect to their product claims:

Applicant should further note that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim(see MPEP 2111.02).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 6 is indefinite over the recitation of "medium-high immobilization density...is less than or equal to 2". This phrase makes the claims unclear because the specification defines the medium high immobilization density on page 9 as when the "ratio (rs) as defined above is greater than 1.7 and less than or equal to 2"(Specification Pg. 9). There is no fixed definition in the art for what constitutes medium-high immobilization density. It is unclear, eg. whether the term refers to the medium-high immobilization density requirement defined in the claim or the specification's definition and why the two would differ. The claims should be amended to clarify to what specific condition "medium-high immobilization density" refers.

B. Claims 6 and 7 are indefinite over the recitation of "ratio r_s". This phrase makes the claims unclear because the specification only defines the ratio as "the mean centre-to-centre

separation distance of the oligomers to the average length of immobilized oligomers". There is no fixed definition in the art for what constitutes "ratio r_s". It is unclear, eg. whether the term refers to the comparison of measurements in Angstrom's, moles, oligonucleotides or the traditional units for density in this regard of moles/cm^2. The claims should be amended to clarify to what specific number/units/proportion they are attempting to claim using the "ratio r_s" recitation.

C. Claim 8 is indefinite over the recitation of "dendritic assembly". This phrase makes the claims unclear because the specification does not define what is encompassed by a "dendritic assembly". There is no fixed definition in the art for what constitutes a "dendritic assembly". It is unclear, eg. whether the term refers to an assemblage of nucleic acids isolated from dendritic cells or a certain configuration of nucleic acids. The claims should be amended to clarify to what specific limitation "dendritic assembly" refers.

Claim Rejections - 35 USC § 102

Applicant should note that the following art rejections are made in light of the claim interpretations section and indefiniteness rejections made above. The claims are broadly drawn to a substrate for hybridization. The claims are replete with broad terms and phrases lacking structurally relevant definitions in the specification e.g. "fully-matched", "mismatched", "low immobilization density", "medium-high immobilization density", and "high immobilization density". The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*,415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir.

1989) (see MPEP 2111). The claims are given the broadest reasonable interpretation consistent with the broad claim language as detailed below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1, 2, 6-17, and 19-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan(US Patent 5,474,796).

With regard to claims 1, 2, and 24, Brennan teaches a substrate for hybridization comprising a plurality of first nucleic acids alone in their teaching of an array that "contains oligonucleotides having 10 nucleotides each(10-mers)"(Col. 9). The array is taught to represent "every possible permutation of the 10-mer oligonucleotide"

With regard to claims 6 and 7, Brennan et al. teach 10 mer oligonucleotides that are spaced at 7 nm intervals to provide an oligonucleotide loading density of 3.4×10^{-12} moles/cm^2 . As the definition of "medium-high immobilization density" is defined in the claim as "less than or equal to 2", and that of high-immobilization density is "less than or equal to 1.7" and no direction concerning the units of length to be used in calculating their ratio is present, 7 nm/10 oligonucleotides < 2, which anticipates both of these claims.

With regard to claim 8, references teaching of hybridization analysis using arrays of trimers as seen in their Figure 1 is interpreted as anticipating the indefinite limitation of a "dendritic assembly".

With regard to claims 9, 10, 11, 12, and 17 the reference teaches in Example 1. Col. 7, that the array's "plate is treated with hexaethyleneglycol and sulfuric acid to convert the glycidyl epoxide into a hydroxyalkyl group, which acts as a linker arm". "The hydroxyalkyl group resembles the 5'-hydroxide of nucleotides and provides a stable anchor on which to initiate solid phase synthesis". "The hydroxyalkyl linker arm provides an average distance of 3-4 nm between the oligonucleotide and the glass surface"(Col. 7 lines 20-40). The reference further teaches in Col. 4, that such "a number of alternative functionalized surfaces can be used in the present invention that include polyethylene/polypropylene functionalized by gamma irradiation or chromic acid oxidation, and reduction to hydroxyalkyl surface" that is above described as the linker for both oligonucleotides and peptides. As a result the above reference anticipates the linker that comprises a polyether moiety, a polyethylene oxide moiety or a polymeric moiety(Col. 4 line 62).

With regard to claim 16, Brennan teaches that nucleic acid arrays as has been stated above, but also the "methods of the invention may be applied to the determination of peptides or peptide mimetics that bind biologically active receptors"(Col. 3 for example, lines 23-35) thus anticipating the claim's limitation of a substrate wherein a plurality of nucleic acids and also oligomers that are not nucleic acids are immobilized on the substrate.

With regard to claims 13, 14, 15, and 22-23 the reference teaches arrays made out of spots on microarray chips of "every possible permutation of the 10-mer oligonucleotide"(Col.

9), which therefore anticipates identical nucleic acids, mixtures of nucleic acids and a substrate meant for hybridization.

With regard to claims 19 and 20, the reference in Col. 9 lines 61-65 that the hybridization between the first and second nucleic acids is performed in a 3M Me_4CCL solution which anticipates the limitation of a high ionic strength solution of at least 0.3M.

3. Claims 1, 2, 9, 10, 11, 12, 17, 18, 22 and 23 are rejected under 35 U.S.C. 102(e) as being anticipated by Thompson et al.(US Patent 6,169,194 B1).

With regard to claim 1, Thompson et al. teaches a substrate for hybridization comprising a plurality of first nucleic acids in Col. 1 lines 9-23, "this invention relates to the preparation of covalently immobilized nucleic acids onto solid supports using a novel trichlorosilane adhesion agent which forms a monolayer film and provides a reactive thiol functionality to which oligonucleotides can be attached in very high density"(Thompson et al.).

With regard to claim 2, 22 and 23 Thompson et al. teach the above substrate wherein a second nucleic acid will selectively hybridize to the first nucleic acid in the teaching in Col. 3 that "detection of oligonucleotides for diagnostic assays through hybridization and sequencing is also dependent on high density surface immobilization of oligonucleotides"(Col. 3 lines 1-38).

With regard to claims 9-12 and 17-18 drawn to the above substrate wherein the nucleic acids are immobilized to the substrate by a polyether moiety, poly(ethylene oxide) moiety or a polymeric moiety linker and furthermore wherein one or more oligomers comprise polymeric moieties or wherein one or more oligomers are polyethers. In col. 4 the reference teaches that "it is most desirable to attach the nucleic acid covalently to the surface by a linker attached to one of

the end of the nucleic acid chain"(lines 32-35). Furthermore, the reference teaches in Col. 8 that "a third aspect of the invention concerns the method by which the linkers are connected to the nucleic acid moiety. Nucleic acids can be synthesized so they contain an integral tether termination in a thiol group. The tether consists of 2-20 units in length, which may be composed of either hydrocarbon or polyether functionalities"(Lines 5-10). It is a further aspect of the invention that "the tether attached to the oligonucleotide is a polyether chain of from 2 to 20 atoms"(Col. 8 lines 65-67).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 3, 4, 5, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brennan et al. in further in view of Breslauer et al(PNAS Vol. 83 pp. 3746-3750 1986).

With regard to claims 1, 2, and 24, Brennan et al. teach a substrate for hybridization comprising a plurality of first nucleic acids alone in their teaching of an array that "contains oligonucleotides having 10 nucleotides each(10-mers)"(Col. 9). The array is taught to represent "every possible permutation of the 10-mer oligonucleotide"

With regard to claims 6 and 7, Brennan et al. teach 10 mer oligonucleotides that are spaced at 7 nm intervals to provide an oligonucleotide loading density of 3.4×10^{-12} moles/cm^2 . As the definition of "medium-high immobilization density" is defined in the claim as "less than or equal to 2", and that of high-immobilization density is "less than or equal to 1.7" and no direction concerning the units of length to be used in calculating their ratio is present, 7 nm/10 oligonucleotides < 2, which anticipates both of these claims.

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described as the linker for both oligonucleotides and peptides. As a result the above reference anticipates the linker that comprises a polyether moiety, a polyethylene oxide moiety or a polymeric moiety(Col. 4 line 62).

With regard to claim 16, Brennan teaches that nucleic acid arrays as has been stated above, but also the "methods of the invention may be applied to the determination of peptides or peptide mimetics that bind biologically active receptors"(Col. 3 for example, lines 23-35) thus anticipating the claim's limitation of a substrate wherein a plurality of nucleic acids and also oligomers that are not nucleic acids are immobilized on the substrate.

With regard to claims 13, 14, 15, and 22-23 the reference teaches arrays made out of spots on microarray chips of "every possible permutation of the 10-mer oligonucleotide"(Col. 9), which therefore anticipates identical nucleic acids, mixtures of nucleic acids and a substrate meant for hybridization.

With regard to claims 19 and 20, the reference in Col. 9 lines 61-65 that the hybridization between the first and second nucleic acids is performed in a 3M Me_4CCL solution which anticipates the limitation of a high ionic strength solution of at least 0.3M.

Brennan et al do not teach measuring the Tm of the oligonucleotides mobilized on their arrays.

However, Breslauer et al. teach predicting DNA duplex stability from the base sequence. Breslauer et al. teach the complete thermodynamic library of all 10 Watson-Crick DNA nearest-neighbor interactions. Most importantly, the reference teaches that "armed with this knowledge and the nearest-neighbor thermodynamic data reported here, scientists now will be able to predict the stability(ΔG°) and the melting behavior (ΔH°) of any DNA duplex structure from inspection

of its primary sequence"(Abstract). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the substrate with every ten mer of Brennan with the specific combination that would yield the desired Tm as instructed by the Breslauer reference for the expected benefit that "this capability should prove valuable in numerous applications such as (i)predicting the stability of probe-gene complex; (ii) selecting optimal conditions for a hybridization experiment; (iii) deciding on the minimum length of a probe etc"(Abstract).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sally A Sakelaris whose telephone number is 571-272-0748. The examiner can normally be reached on Mon-Fri, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sally Sakelaris

2/17/2004

JEFFREY FREDMAN
PRIMARY EXAMINER